REMARKS

Claims 1, 2, and 39-41 are pending. In the Office action mailed January 8, 2009, claim 2 is objected to. Claims 1, 2, and 39-41 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent Application Publication No. 2006/0099578 ("the '578 publication"), as evidenced by U.S. Patent No. 5,494,794 ("the '794 patent"). Claims 1 and 39-41 are also rejected under 35 U.S.C. § 103(a) as being obvious over the '794 patent in view of U.S. Patent No. 6,040,138 ("the '138 patent"). Claims 1 and 39-41 are also rejected under 35 U.S.C. § 103(a) over Smeitink et al., Human Mol Genet 7:1573-1579, 1998 ("Smeitink") in view of the '138 patent. Each of these rejections is addressed below.

Interview summary

The undersigned thanks Examiner Salmon for the helpful telephone interview on March 11, 2009. Discussed were proposed amendments to the claims, as well as the anticipation and obviousness rejections in view of the amended claims.

The invention

The present inventors have discovered that expression of *nuclear encoded* mitochondrial energy metabolism genes is decreased in patients suffering from bipolar disorder. In view of this discovery, the present invention is directed to a microarray consisting of at least 90% nucleic acid molecules that either (a) encode polypeptides of complex I, II, III, IV, or V of the mitochondrial respiratory chain, which are naturally coded for by a *nuclear gene*, or (b) are fragments of (a). The claimed arrays can be used, for example, to diagnose bipolar disorder in a patient or to determine the patient's propensity for developing bipolar disorder.

Claim objection

Claim 2 stands objected for reciting nonelected subject matter. Because claim 1 is under consideration and generic with respect to the nucleic acid molecules recited in claim 2, Applicants request that this objection be held in abeyance.

Rejection under 35 U.S.C. § 102(e)

Claims 1, 2, and 39-41 stand rejected under § 102(e) as being anticipated by the '578 publication, as evidenced by the '794 patent. In making this rejection, the Office asserts that the '578 publication teaches a microarray consisting of probes for mitochondrial genes, in particular, mitochondrial energy genes.

Further, the Office asserts that claimed microarray is not limited to at least 90% nucleic acid molecules that encode polypeptides naturally coded for by a nuclear gene. Applicants respectfully disagree with the Office on this point. However, the Office suggests that this rejection can be overcome by amending claim 1 to recite "a microarray consisting of at least two nucleic acid molecules." Applicants have therefore amended claim 1 as suggested by the Office. Withdrawal of the rejection of claim 1 and dependent claims 2 and 39-41 is respectfully requested.

Rejection under 35 U.S.C. § 103(a) – the '794 patent in view of the '138 patent

Claims 1 and 39-41 are also rejected as being obvious over the '794 patent in view of the '138 patent. In making this rejection, the Office notes that the '794 patent teaches probes to detect mutations in mitochondrial DNA, and that defects in oxidative phosphorylation may play a role in the pathogenesis of Alzheimer's disease and Parkinson's disease. The Office therefore concludes that the '794 patent teaches probes related to oxidative phosphorylation. As the '794 patent does not teach placing oligonucleotide probes onto an array to detect expression, the '138 patent is cited as providing this teaching.

As above, the Office contends that the claimed microarray is not limited to nucleic acid molecules where at least 90% of the nucleic acid molecules encode a polypeptide naturally coded by a nuclear gene. Again, Applicants respectfully disagree with the Office on this point. Nonetheless, Applicants have amended claim 1 to recite "a microarray consisting of at least two nucleic acid molecules," as suggested by the Office. In view of this amendment, the rejection over the '794 patent in view of the '138 patent may also be withdrawn.

Rejection under 35 U.S.C. § 103(a) – Smeitink in view of the '138 patent

Claims 1 and 39-41 are also rejected as being obvious over Smeitink in view of the '138 patent. In making this rejection, the Office asserts that Smeitink teaches that complex I of the mitochondrial respiratory chain includes nuclear genes. Smeitink is also asserted to teach that mutational analysis of nuclear encoded subunits has implications for genetic counseling. Because Smeitink does not teach an array, the '138 patent is cited as providing this teaching. Based on these teachings, the Office asserts that it would be prima facie obvious to bind probes of the mitochondrial respiratory chain taught by Smeitink to an array of the '138 patent, because one would want to determine changes in the nuclear genes of human complex I.

Applicants respectfully traverse this rejection. As an initial matter, Smeitink is silent with respect to making an array. There is simply no teaching in Smeitink indicating that it would be advantageous to include mitochondrial complex I nucleic acids on an array. For this reason, the combination of Smeitink and the '138 patent cannot render the present claims obvious.

Notwithstanding the failure of Smeitink to teach an array, were one to produce an array based on the nucleic acids taught in this reference, one would *not* produce an array of claim 1. Smeitink is entirely concerned with genetic/mutational analysis of complex I proteins and the relationship between these proteins and *metabolic defects* caused by

complex I deficiencies. See, e.g., Smeitink, page 1573, column 2. Because complex I is made up of subunits encoded by both nuclear and mitochondrial genes, mutations in any of these genes can lead to complex I deficiencies. Smeitink, page 1576, column 2, second paragraph. Indeed, Smeitink teaches that a number of mutations in mitochondrial encoded genes are involved in such complex I metabolic deficiencies.

Accordingly, an array useful for analysis of the complex I genes involved in Smeitink's *metabolic deficiencies* would necessarily include both the nuclear-encoded and mitochondrial-encoded genes of complex I. An array that omits certain mitochondrial genes (e.g., the array of claim 1) would in fact preclude a full genetic analysis of the complex I genes from being performed, and thus would not be useful in genetic analysis of complex I metabolic disorders. By contrast, the arrays of the present invention only require nuclear-encoded genes, and indeed require that 90% of the nucleic acid molecules on the array encode polypeptides naturally coded for by a nuclear gene, or fragments thereof. Thus, the teachings of Smeitink, either alone or in combination with the '138 patent, fail to teach the claimed arrays, and this combination of references cannot render claim 1 or its dependent claims obvious.

For all of these reasons, withdrawal of the obviousness rejection over Smeitink in view of the '138 patent is respectfully requested.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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